UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/042,417	01/07/2002	Michele Pagano	5914-090-999	1343

20583 7590 10/16/2006

JONES DAY
222 EAST 41ST ST
NEW YORK, NY 10017

EXAMINER	
CANELLA, KAREN A	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 10/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/042,417	PAGANO, MICHELE	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-3,7-9 and 22-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-3,7-9,22,25 and 26* is/are rejected.

7)☐ Claim(s) *23, 24* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 4-6 have been canceled. Claims 1, 3, 7 have been amended. Claims 22-26 have been added. Claims 1-3, 7-9 and 22-26 are pending and under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 requires that the Cks1 is purified from an in vitro translation reaction or recombinant expression system. It is unclear at what point in the claimed method said purification is to take place. It is unclear if applicant is intending to limit the claim to reaction mixtures having as a constituent in vitro purified Cks1.

Claims 1-3, 7-9, 25 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carrano et al (Nature Cell Biology, 1999, Vol. 1, pp. 193-199) as evidenced by Ganoth et al (Nature Cell Biology, 2001, Vol. 3, pp. 321-324).

Claim 1 is drawn to a method for screening for a compounds useful for the treatment of proliferative and differentiative disorder comprising contacting a test compound in vitro with a reaction mixture comprising Skp2, p27, Cdk2 and Cks1, and detecting a change in Skp2-binding activity or Skp2-ubiquitin ligase activity. Claim 2 embodies the method of claim 1 wherein the change in Skp2 binding activity is detecting by detecting a change in the binding of Skp2 with either p27 or Csk1. Claim 3 embodies the method of claim1 wherein the change in Skp2-ubiquitin ligase activity is detected by detecting a change in the ubiquitination or degradation ofp27 of Cks1.

Claim 7 is drawn to a method for screening for a compound useful for the treatment of proliferative and differentiative disorders comprising contacting a test compound with a reaction mixture containing Skp2, Cks1 and a polypeptide comprising the carboxyl terminus of the human p27 chain of SEQ ID NO:91, with or without a phosphothreonine at position 8 and

detecting a change in the interaction of Skp2 with Cks1 or detecting a change in the interaction of Skp2 with the polypeptide comprising SEQ ID NO:91 (p27). Claim 8 embodies the method of claim 7 wherein the change in the interaction of Skp2 with Csk1 or the polypeptide is detected by detecting a change in the binding of Skp2 to either Csk1 or the polypeptide.

Claim 9 embodies the method of claim 7 wherein the change in the interaction of Skp2 and Cks1, or a change in the interaction of Skp2 and the polypeptide comprising SEQ ID NO:91 (p27) is detected by detecting a change in the ubiquitination or degradation of said polypeptide.

Claims 25 and 26 embody the method of claim 2 wherein the change in binding of Skp2 to p27 is detected by detecting an increase in binding and a decrease in binding, respectively.

Carrano et al teach that Skp2 is required for ubiquitin mediate degradation of p27. Carrano et al teach that the combined addition of Skp1-Skp2 and cyclinE-CDK2 to G1 extracts of HeLa cells markedly stimulated p27 proteolysis (page 195, first column, lines 16-23). Carrano et al teach that Skp2 and Cyclin E-cdk2 are rate limiting for p27 ubiquitination on G1 extracts (legend for Figure 3). Carrano et al teach that in many cancer cell lines, Spk2 levels are high and that a specific small-molecule inhibitor of Skp2 should increase the cellular abundance of p27 and lead to a block in cellular proliferation and disease progression (page 198, last paragraph).

The HeLa cell extracts used by Carrano et al comprise Cks1 as evidenced by Ganoth et al who teach that Cks1 is present in HeLa cell extracts (lines 9-12 of abstract, and lines 10-11 in the first paragraph under the abstract).

It would have been prima facie obvious at the time the claimed invention was made to screen for a specific small-molecule inhibitor of Skp2 which would increase the cellular abundance of p27 by measurement of the interaction between Skp2 and p27 measured by Skp2-binding to p27 or the resulting proteolysis of ubiquitinated p27 by adding a candidate small molecule inhibitor to HeLa G1 extracts comprising adding Skp1-Skp2 and cyclinE-CDK2 to said extracts and contacting the mixture with a candidate inhibitor. One of skill in the art would be motivated to do by the suggestion of Carrano et al that a small molecule inhibitor of Skp2 would result in increased levels of p27 and concomitant decrease in cellular proliferation. Carrano et al fulfill the specific limitation of the claims with regard to composition and Skp2 binding or ubiquitin ligase activity because the Cks1 is inherently present in the mixture.

Carrano et al fulfill the specific limitation of claims 2, 5, 7, 8, 9, 10, 14, 17 with respect to the binding of Skp2 because Cks1 is listed in the alternative. Carrano et al fulfill the specific limitation of claim 7 and 9 with regard to a polypeptide corresponding to the carboxyl terminus of the human p27 protein because one reasonable interpretation of "corresponding to" said protein is the full length p27 protein.

Applicant argues that the teachings of Carrano et al fail to fulfill the embodiments of the instant invention, because Carrano et al fail to teach the in instant in vitro reaction mixture using purified components. This has been considered but not found persuasive. A reaction mixture using HeLa cell extracts constitutes an in vitro system.

Claims 1-3, 7-9, 25 and 26 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 20-22 of copending Application No. 10/632,150 in view of Carrano et al (Nature Cell Biology, 1999, Vol. 1, pp. 193-199). New claims 25 and 26 are also rejected.

The instant claims are obvious over the claims 20-22 of '150 in view of Carrano et al who teach that Skp2 is required for ubiquitin mediate degradation of p27. One of skill in the art would have been motivated to detect the "activity" of Skp2 by measured by ubiquitination or proteolysis of p27 which is taught by Carrano et al.
This is a provisional obviousness-type double patenting rejection.

All other rejections and objections as set forth in the previous Office action are withdrawn in light of applicants amendments and arguments.

Claims 23 and 24 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Karen A. Canella, Ph.D.
10/1/2006

KAREN A. CANELLA PH.D
PRIMARY EXAMINER